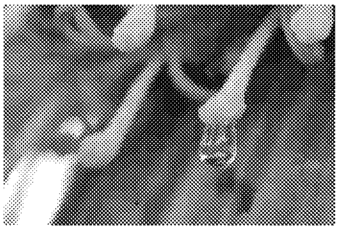
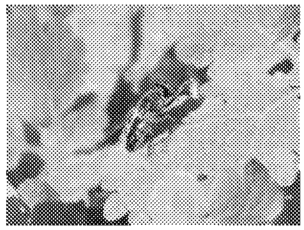
  

# Neonic Risk Assessments – Final Bee, Aquatics, & Terrestrial

(Clothianidin, Dinotefuran, Imidacloprid, and Thiamethoxam)

EFED Briefing for OCSPP AA

September, 2019

# Outline of Presentation

- Background
- Final Bee Risk Assessments
  - Approach for assessing risks to bees
  - New Data/Methodologies
  - Risk conclusions
- Risk conclusions for birds and mammals
- Risk conclusions for aquatic taxa & new comparative analysis
- Conclusions/Next Steps




Goal is:
Provide OCSPP management with a summary of neonic risk conclusions final bee risk assessments and the aquatic and terrestrial taxa (non-bee) risk assessments

Emphasize new methodologies and the incorporation of public comments received on the preliminary bee assessments from 2016 in the final bee assessments

Provide detailed scientific background prior to PRD's briefing on the neonic risk mitigation strategy

# What are Neonicotinoids?

- A class of systemic insecticides, first introduced in the U.S. in the 1990s
- All neonics have a mode of action as agonist of the nAChR receptor
- Different classes of nAChR agonists:
  - Nitroguanidine-substituted neonicotinoids includes: imidacloprid, clothianidin, thiamethoxam, and dinotefuran
  - Cyano-subsituted neonicotinoids (*e.g.* acetamiprid)
  - Sulfoxaflor is considered its own sub-category (non-neonicotinoid)
- High public interest
  - Large number of studies (open literature and registrant submitted)
  - Incidents (beekills) relating to exposure from seed dust off
  - > 1 million comments received on our preliminary RAs



These agonists act on an insect's central nervous system and they may have lethal effects, but also a range of sublethal effects in insects such as effects on vision/smell, learning and memory.

# Neonic Registration Review Timing

- Problem Formulations
  - Imidicloprid (IMI) published December, 2008
  - Clothianidin (CLOTHI), Thiamethoxam (THIA), Dinotefuran (DINO) published December, 2011
- Preliminary Bee Risk Assessments
  - IMI published January 2016, CLOTHI / THIA, DINO published May 2017
- Non-Bee Risk Assessments
  - IMI published September 2017, CLOTHI/THIA, DINO published December 2017
- Final Bee RAs, RTC, and Proposed Interim Decisions
  - Incorporates pubic comments (USDA, industry, academia, grower groups) received on the Preliminary RAs
  - Signatures Pending
  - Dockets to open shortly thereafter



Just a quick overview of the registration review timeline and a reminder that although the 4 neonics started registration review at different times, they have all been aligned during the risk management phase. We're going to use these abbreviations throughout the presentation.

It's worth noting that clothianidin is a degradate of thiamethoxam that forms in plants after thiamethoxam application.

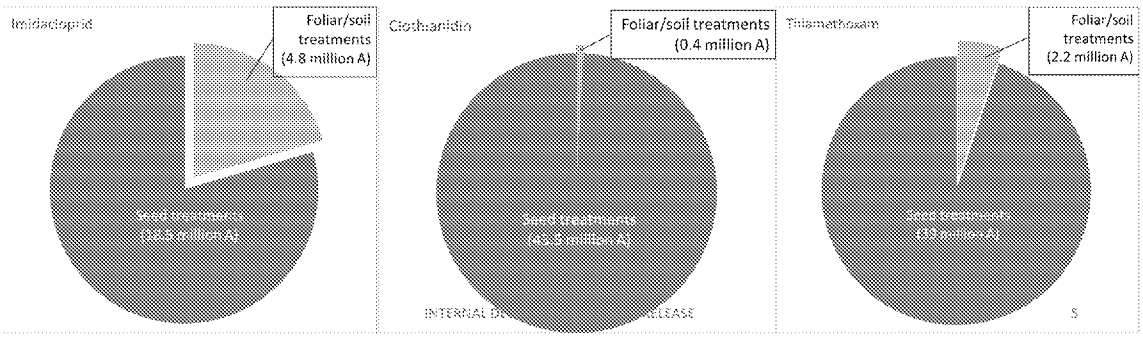
Also- just to orient you to the overall timing for the pollinator work, we went to the SAP in 2012 and finalized our guidance in 2014 so these assessments are really among the first refined risk assessments EFED has done for bees using the new methods.

Public Comments following preliminary Bee RAs: we specifically requested comment on the method for evaluating effects from the pollen route of exposure. We received a number of helpful comments that we used to refine the method used in the Final risk assessments, which we will go over with you later.

Data generation by the registrants was conducted simultaneous with our efforts to create guidance. Sometimes this helped sync up the data we received to our needs really well. Other times, data might not have sync'd well (for example, early bee studies might not have been as good as studies we get now that now have established guideline recommendations and criteria)

# Neonicotinoid General Use and Usage

- Registered for variety of crops, but primarily (by Lbs and acreage) as seed treatments for IMI, CLOTHI, THIA
  - Corn and soybeans represent majority of usage
  - No registered seed treatments for DINO




Let's quickly discuss the actual usage of these chemicals, which are widely used across the country on many agricultural crops with different use patterns as well with non-Ag uses such as ornamental, forestry and poultry house structures.

IMI, CLOTHI and THIA are registered as seed treatments for a variety of crops, while DINO has no seed treatment uses. The three pie graphs show the average acres treated of seed treatments versus all other uses registered for IMI (80%), CLOTHI (99%), and THIA (95%). These highlight just how much of the use is seed treatment.

We haven't included dino on this chart, bc it's use is significantly less, ~25K lbs, with about a ¼ of that on cucurbits and another ¼ on rice.

# Overall Bee Risk Conclusions

- **Final bee assessments:**
  - Risk to bees greatest for foliar treatments and least for seed treatments
    - Potential impacts on pollination services and species biodiversity
    - Risks are based on impacts to colonies with foragers bringing back exposed nectar and pollen from the treated field
  - Highly refined assessments
    - Include new methods to maximize available data and inform potential mitigation
    - Responsive to public comments
  - Risk depends on use site, application method and chemical-specific factors
  - Off-field Risks include Seed Dust Off, Spray Drift, Treated Poultry Litter

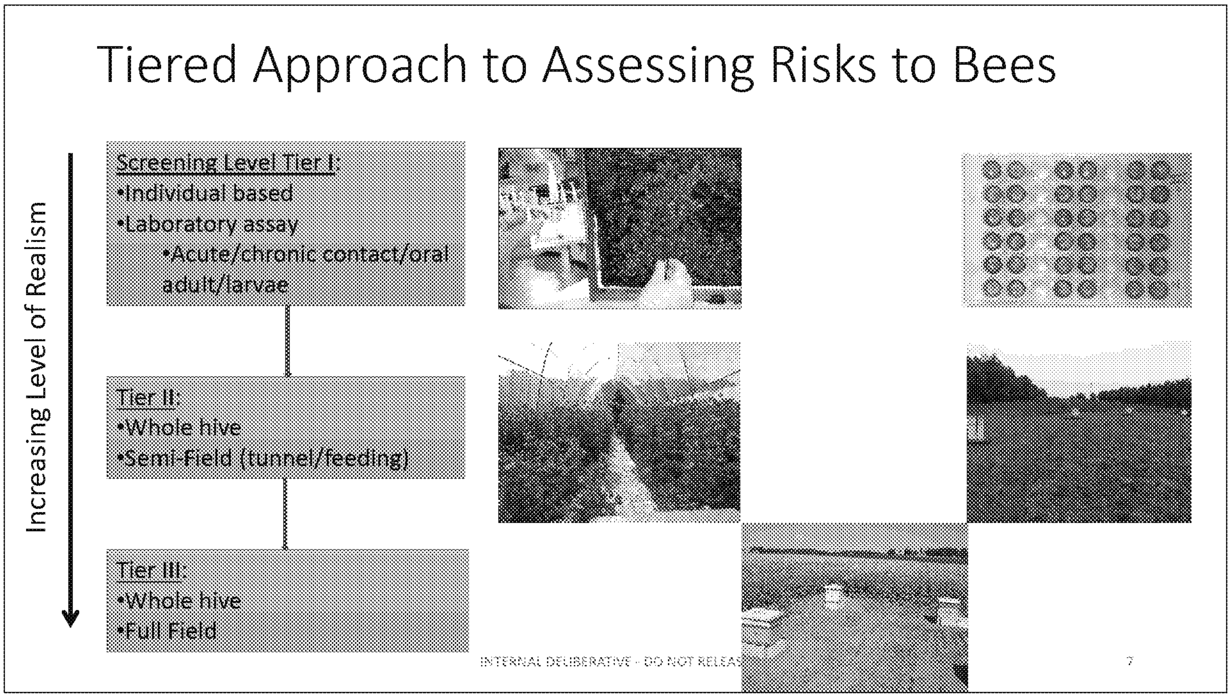


These RAs considered both Ag and Non-Ag Use sites (e.g. Ornamentals)

We found that risks were Fol>Sol>Seed Treatment.
Potential Impacts on our Pollinator Protection Goals of Pollination Services and Species Biodiversity.
Most of the conclusions we are presenting today are for colony-level risk based on impacts to colonies exposed to nectar and pollen that have been brought back to the hive from the treated field

Highly Refined RAs that are data-rich and allow for increased levels of realism and refinement. Include some new methods which we'll discuss shortly and maximize the use of all this data and are responsive to public comments we received following the preliminary bee risk assessments in 2016

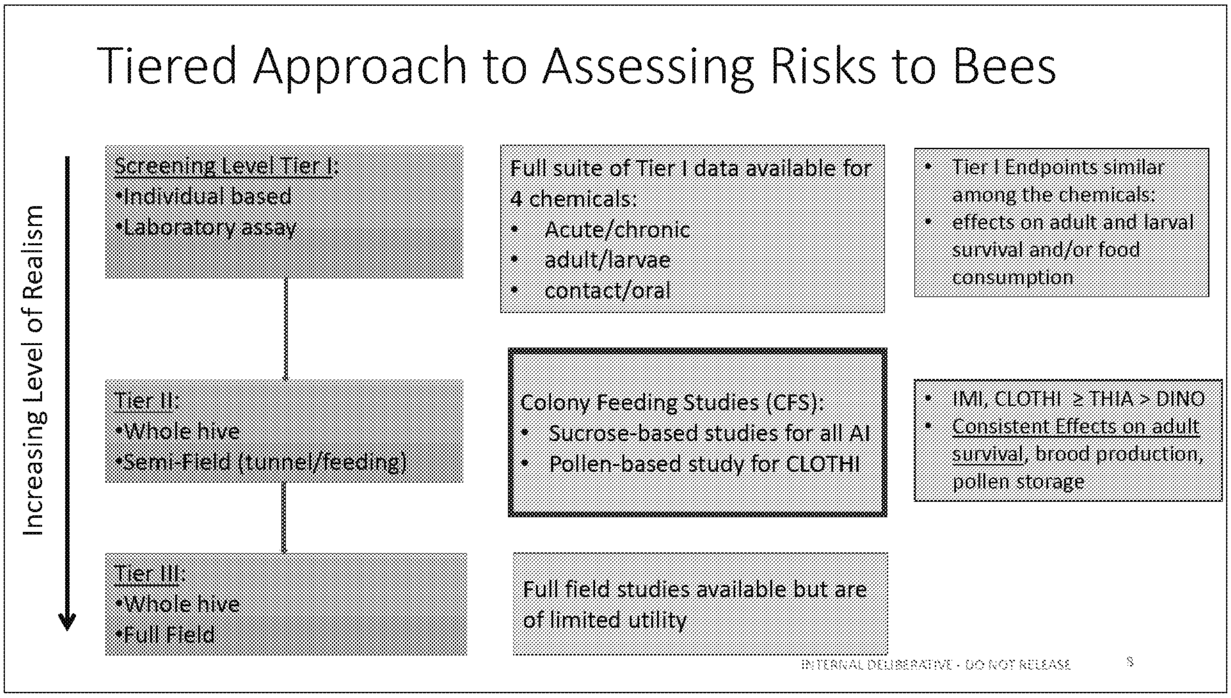
We're not going to discuss the off-field risks very much in this presentation, but given the concerns over seed dust off I want to acknowledge the issues with this, we've received a relatively large number of incidents following the planting of treated seed (typically corn) and the resulting movement of dust containing very high residues from the seed treatment moving off the field and affecting beekeepers. Due to legal (seed is the treated article) and technical reasons (haven't developed away to model dust off), it is not quantitatively assessed in our risk assessments and the goal is to manage this through stewardship.




I think we've described our bee risk assessment approach in the Sulfoxaflor briefing you had a few months ago, but for a quick recap--Risk to bees is assessed with a tiered approach that is designed to allow for increasing levels of realism and refinement for both toxicity and exposure as you move up the tiers. I'll note that before we even start with tier 1, we consider potential for exposure using USDA bee attractive guidance. Those crops that are not pollinator attractive are still evaluated for potential off-field effects (e.g., from spray drift). For pollinator attractive crops, the screening level, or Tier 1, is based on lab studies at the individual bee level. Tier 2 evaluates the whole hive with semi-field tunnel/feeding studies. These studies, particularly the CFS studies can be quite costly to perform due to the large level of replication needed to conduct them. And finally, Tier 3 evaluates the whole hive with full field study(s).

On the exposure side, at the Tier 1 level we use conservative modeled values for on-field exposures. These default estimates of exposure can then be refined using available chemical-specific residue data. I also want to note here that even at the refined Tier I level, almost all foliar and soil uses and even some seed treatments would have risk indicated. But, at the Tier II level, we were able to make many more differential risk calls.

Also at the Tier 1, we use conservative models for spray drift to evaluate potential off-field exposures.




At the Tier I tox level, we have the full suite of laboratory studies for all 4 chemicals.

We also have over 80 registrant-submitted studies with empirical residue data following neonic applications.

At the Tier II level, we have registrant-submitted feeding studies for all four chemicals based on spiked sucrose exposure (considered an analog of nectar exposure) and we had some colony level data for spiked pollen patty exposures for clothianidin. Based on these studies, IMI and ClOTHI had the most sensitive endpoints (NOAEC/LOAECs) based on consistent effects to adult survival, brood production and pollen stores in the colony over multiple measurement time points. THIA was a bit less sensitive and then DINO was not very sensitive, with no consistent effects.

We also had one pollen-based study for CLOTHI, which was very helpful for considering effects based on pollen exposures.

At the Tier III level, Several full field studies are available, but many confounding factors in them and in the end they are of limited utility.
Given the inherent uncertainties associated with the available Tier III data, the risk calls of no risk or risk is based on the Tier II effects data and the empirical exposure data, although the Tier III studies are considered as a line of evidence in our risk calls.

# New Methodologies

Developed based on public comments received on draft assessments:

- Pollen Method
- Residue Bridging Method
- Weight of Evidence Method



In the next few slides we'll discuss our new methodologies, which include a pollen method to incorporate the potential exposure of honey bee colonies to residues in both nectar and pollen, a residue bridging method to be able to bring in residue data across crops, crop groups and chemical and a weight of evidence approach that allowed us to state our confidence when we indicate there is potential risk to honey bee colonies on a scale from weak to strong evidence.

## Nectar + Pollen Total Dietary Exposure

- Honey bee colonies consume both nectar and pollen, yet our CFS endpoints are based on sucrose (nectar) exposure only
- A method was needed to incorporate additional exposure from pollen
  - Proposed approach in Preliminary RAs vs. Final Approach
- Multiple lines of evidence suggest:
  - Pollen residues can be divided by 20 to convert pollen exposures to nectar exposure equivalents



We'll start with the nectar equivalents method. Bees can be assessed to residues in both nectar and pollen. Evaluating the nectar route of exposure is very easy, you just compare you sucrose-based NOAEC endpoint to the concentration in nectar. Evaluating the pollen route of exposure is more difficult, since we generally don't have colony feeding studies based on pollen exposure (again, Tier II colony feeding studies are really expensive and getting 2 large scale ones for each chemical can be prohibitive).

It's important to note that residues in pollen can be much higher (on the order of 10x) nectar residues, but we know that as a whole, bees consume much more nectar than pollen as a colony, but the exact proportions differ depending on the bee caste (nurse bees consume relatively higher amounts of pollen then other bees, while foraging bees consume almost none).

We had many public comments from registrants, USDA and academia on our previous method used in the Preliminary Bee RAs (the bee bread method). As a result of these comments as well as additional data submitted by the registrants, we went back and re-evaluated how to address pollen exposures.

The Tier II pollen and nectar method is a way of combining measured concentrations for both matrices into a concentration in total diet that essentially converts residues in pollen to nectar equivalents by the application of a 20x factor. This factor was determined by evaluating separate lines of evidence to determine the relative contribution of pollen to colony-level exposure and was supported by the limited Tier II toxicity data for pollen exposures.

This approach is consistent with the approach proposed by industry in their comments on our draft RAs which essentially said, "you need to use some sort of factor to convert pollen exposures to nectar exposures based on bee consumption rates", rather than the approach we used in the preliminary risk assessments which was very complicated and overly conservative.

As a result of our analysis, other risk assessments have started to use this approach, most notably the sulfoxaflor Bee RA you were briefed on.

# Residue Bridging Strategy-General Trends

- Residues from foliar applications > soil applications > seed treatments
  - Residues from foliar applications = 100 - 1000s ppb
  - Residues from soil applications = 10 - 100s ppb
  - Residues from seed treatments = 1 - 10s ppb
- Although residues from foliar applications are generally higher in magnitude, they decline more rapidly than soil applications (which tend to persist in pollen and nectar for much longer time periods)
- Pre-bloom applications result in residues that are generally much higher than post-bloom applications
- Data generally supported extrapolation of residues across neonics, but not among application methods
  - Within an application method and crop group, residues extrapolated among crops
  - In absence of data for a given crop group, considered all data within an application category (*e.g.* use all herbaceous crop data for herbs and spices crop group)




We had over 80 studies across all the ai and crop groups to assist in this bridging strategy, many of which were submitted after the preliminary bee risk assessments and we conducted a detailed analysis of the residue data to support extrapolations among crops and chemicals when needed. We followed a crop group approach similar to that used in our human health risk assessments.

This strategy allowed us to make the best use of the available residue data to 1) distinguish between our "low risk" and our "risk" calls with some level of confidence, and also 2) gives us the ability to inform on potential mitigation options, e.g., a pre-bloom interval that would preclude potential risk.

Based on these analyses we saw some general trends in the data. At the 30,000 foot level, residues from foliar applications are greater than residues from soil applications, which are greater than residues from seed treatments. I'll note that the range of residues presented for foliar applications is based on samples taken close to application (~2 weeks) and approach ppm levels, which is really high levels for insecticides. After that the second bullet comes into play because residues from foliar applications tend to decline much more rapidly than residues from soil applications. Generally there is also a distinction between pre-bloom and post-bloom applications, with residues in flowers following pre-bloom applications being much greater than when they follow post-bloom applications.

Based on these general trends we decided to separate foliar and soil applications as well as pre-bloom and post-bloom applications. You'll see how this factors into the risk calls in a few slides.

Data generally supported extrapolation of residues across neonics, but not among application methods
Within an application method and crop group, residues are extrapolated among crops.
In absence of data for a given crop group (which still happened, despite these 80+ studies), we considered all data within an application category (e.g. to evaluate foliar risks to herbs and spices we extrapolated from all the foliar data from all the herbaceous crops).

Finally, please note that although this is a new approach for our risk assessments, it was also used recently in the Sulfoxaflor Bee RA as a reasonable way to bridge residues.

# Risk Calls and Weight of Evidence Approach

- Risk calls are for each chemical, application and crop group combination

(*e.g.* THIA foliar use on cucurbits)

- Crop attractiveness to bees and agronomic practices (USDA Determination)
- Measured residues greater than adverse effects level for hives (residues above CFS NOAEC and LOAEC)
  - Considered duration and frequency of exceedance
  - Considered magnitude of exceedance
    - Ratio of max residue value to NOAEC/LOAEC
    - % of diet from the treated field needed to reach the NOAEC/LOAEC
  - Considered usage and geographic scale/spatial distribution of exposure
- Reported incidents



As previously mentioned multiple lines of evidence were considered in making risk calls for both low risk/risk and for our confidence in the risk call.

At Tier I, we considered whether the crop was honey bee attractive (based on USDA guidance), as well as any agronomic practices that may limit exposure, e.g., harvest time or flower tenting to prevent bee pollination (as in the case of mandarin oranges). At Tier I we also considered whether predicted or measured residues exceed the individual effect level endpoints, which they mostly did.

At the Tier II level, to determine honey bee colony-level risk, we considered whether residues exceeded the colony level endpoints. This was the major basis for a risk call; however, we provided several additional pieces of information to better characterize the potential for risk, including whether the exceedances were based on chemical specific or bridged residue data; the duration, frequency, and magnitude of the exceedance (which were key considerations given the fate characteristics of these chemicals that contribute to their persistence and systematic movement through plant tissues).

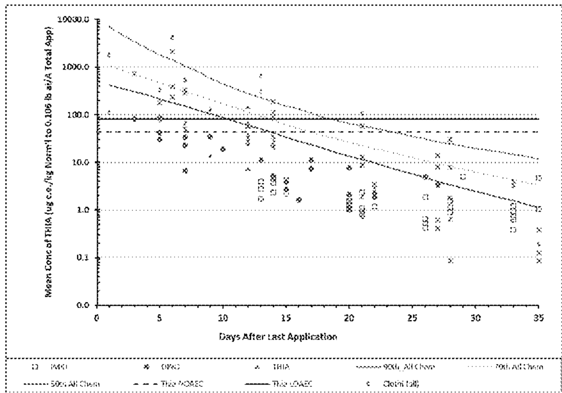
We also considered the geographic scale and spatial distribution of each use pattern. And then we also considered available incident data. The teams incorporated this additional characterization into a discussion of the strength of the risk call for each crop group within a chemical (describing the strength of the evidence as strong, moderate and weak).

I should note, since we've referred several times to the sulfoxaflor assessment, that our strength of evidence calls were not used in that assessment, mostly bc they had much less residue data than we have.

# Strong Evidence of Risk

- Residues exceed colony-level endpoint(s) by a high magnitude, frequency, and/or duration
- Chemical-specific or robust bridged residue data set available
- Residues exceed across multiple locations
- May be supported by modeled (*e.g.*, Monte Carlo) exposures or ecological incidents
- These calls were more likely for foliar applications that had rapid declines so pre-bloom intervals could be determined

Residues in cotton extrafloral nectar following foliar thiamethoxam applications vs. thiamethoxam colony endpoints






Foliar applications to cotton was one example where we determined that the weight of evidence was strong.

In this case, we had a robust dataset with residue data for imidacloprid, clothianidin, dinotefuran and thiamethoxam (each symbol represents a different active ingredient and each data point represents a mean residue sample at a given location and time)

This large dataset allowed us to generate Monte Carlo probabilistic curves representing the 50th(lowest diagonal line) 70th and 90th percentile curves (highest diagonal line) and then we can compare those lines to the colony level endpoints (the horizontal lines, which represent the NOEC and LOEC for thiamethoxam to honey bee colonies).

As you can see, we have really high residues at the start that are several orders of magnitude above the colony endpoints and lower residues later. Also note that even the median (50th percentile) curve exceeds the colony level endpoints for multiple weeks.

# Moderate Evidence of Risk

- Residues exceed colony-level endpoint(s) but:

- limited magnitude, frequency, and/or duration
- Residues exceed across few locations
- Supported by limited incident information
- <u>More often represented by soil applications</u>
  - Driven by application rates
  - Risk call unaffected by application timing

Residues in cucurbits following clothianidin soil applications vs. clothianidin CFS endpoints

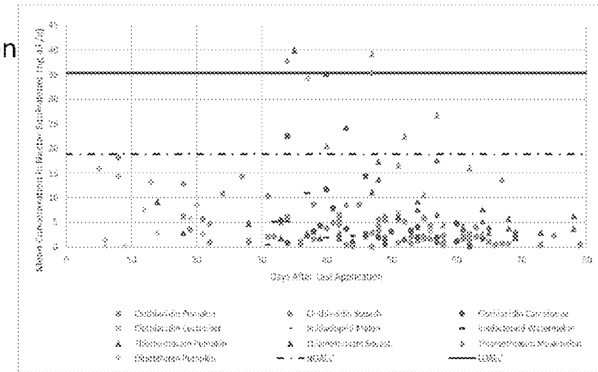




Figure on the right shows neonicotinoid residues in cucurbits (pumpkin, squash, melon and canteoupe). Again, each symbol represents a different chemical and in this case each color represents a different crop.

In this case, neonic residues rarely exceeded the LOAEC and infrequently exceeded the NOAEC, but no conclusions can really be drawn based on application timing as there are no obvious trends in the data.

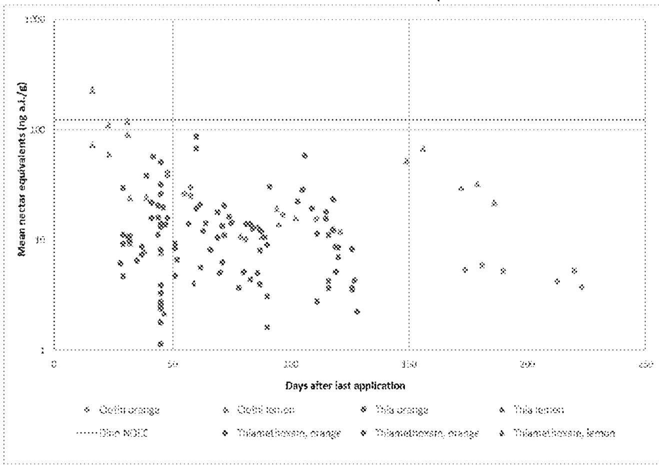
Residues did not exceed CFS endpoints at all 3 sites for any tested crop

I want to note that the thiamethoxam soil cucurbit figure looks very similar, but with the higher endpoints reflected from the thia CFS study and consequently almost no exceedances. Despite this, it was also considered moderate strength of evidence, rather than weak due to available incident data for thiamethoxam.

# Weak Evidence of Risk

- Residues exceed colony-level endpoint(s) but there are uncertainties in the surrogacy in the bridged residue data set
- Vast majority of residues below toxicity endpoint
- Residues exceed at single location
- Not supported by ecological incidents

Residues in orchard crops following soil applications vs. the dinotefuran CFS endpoint







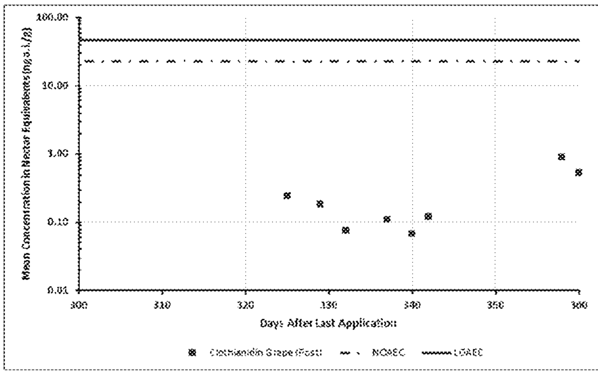

One example of this is pictured at right where for orchard crops following soil applications, we only had one mean residue sample above the dinotefuran colony level endpoint.

Another example is mint (herbs and spices crop group) for thiamethoxam foliar applications. No empirical data for this crop group, so we bridged from all other herbaceous crops: cotton, cucurbits and soybeans. Risk would have been indicated from cotton and cucurbits, but not from soybeans. Given the uncertainty of the relevancy of surrogacy from these crop groups, we determined this was weak evidence.

# Low Risk Calls

- Harvested prior to bloom
  - Bulb, leafy and brassica vegetables; artichoke and tobacco
- Not attractive to honey bees
  - Root and tuber, fruiting vegetables (majority)
- Residues below the colony-level effects endpoint
  - Most seed treatments (incl. corn & soybean)
  - Foliar applications:
    - Legumes
    - post-bloom applications
      - Berries and small fruits
      - Orchards (except IMI stone and pome)
  - Soil applications:
    - Dinotefuran on cucurbits

Residues in berry and small fruits following post-bloom foliar applications vs. the imidacloprid endpoints






Crops/crop groups were considered low risk because they were harvested prior to bloom, not considered attractive to honey bees, or had measured residues below the colony-level effects endpoints. The figure on the right is an example of the latter, where for foliar post-bloom applications to berry and small fruit crops, the residues are substantially lower than the imidacloprid colony level NOAEC and LOAEC.

These low risk calls are for on-field oral exposure only. They are not considering drift off-field or off-field dust off in the case of fugitive dust.

Just to be clear, and to distinguish from the previous slide on weakest, low risk in our assessment means we think the potential for risk is low while weakest on the previous slide indicates that risk potential may in some cases actually be high, but our certainty in the risk call is low due to relatively little evidence or uncertainties in the bridging.

# Low Risk Calls

**Foliar and Soil Applications**

| Crop Group or Crop | IMI | | CLOTHI | | THIA | | DINO | |
|---|---|---|---|---|---|---|---|---|
| | Foliar | Soil | Foliar | Soil | Foliar | Soil | Foliar | Soil |
| Bulb Vegetables | | | | | | | | |
| Leafy Vegetables | | | | | | | | |
| Brassica Vegetables | | | | | | | | |
| Legumes | | | | | | | | |
| Cereal Grains | | | | | | | | |
| Cucurbits | | | | | | | | |
| Citrus Fruits | ** | ** | Post- | Post- | Post- | Post- | | |
| Pome Fruits | | | Post- | | Post- | | | |
| Stone Fruits | | | Post- | | Post- | | Post- | Pre-/Post- |
| Tree Nuts | Post- | | Post- | | Post- | | | |
| Tropical Fruits | | | Post- | | Post- | | | |
| Berries/Small Fruits | Post- | Post- | Post- | Post- | Post- | Post- | Post- | Post- |
| Root/Tubers* | | | | | | | | |
| Fruiting Veg* | | | | | | | | |

**Seed Treatments**

| Crop Group or Crop | IMI | CLOTHI | THIA |
|---|---|---|---|
| Bulb Vegetables | | | |
| Leafy Vegetables | | | |
| Brassica Vegetables | | | |
| Legumes | | | |
| Cereal Grains | | | |
| Oilseed | | | |
| Cucurbit Vegetables | | | |
| Root/Tuber Vegetables* | | | |

* Denotes call is for non-attractive crops
** Mandarin Orange Crop tented during bloom

This table summarizes the low risk calls for foliar and soil applications, represented by green cells. The gray cells indicate either the chemical is not registered for a particular use or there was a risk call (we'll get to those soon). For orchards and berries and small fruits, risk calls are distinguished for pre-bloom vs. post-bloom applications, which was a recommendation from the residue bridging strategy.

Just to reiterate from the last slide, crop groups were considered low risk because they were harvested prior to bloom (top rows), not considered attractive to honey bees (most, but not all crops in the bottom two rows), or had measured residues below the colony-level effects endpoints (middle rows).

Also, I want to note that the low risk call for IMI citrus is only for mandarin oranges, which are tented… all other citrus are high for both foliar and soil applications.

ADVANCE SLIDE: The table on the right summarizes the low risk calls for seed treatments, which accounts for the large majority of usage for imi, clothi, and thia. So things like soybean, corn, which are major uses for these chemicals, were identified as low risk (again, not accounting for potential exposure from dust-off)

Some of these crops were "uncertain" in the preliminary assessments, but the additional data generated for these 3 chemicals allowed us to make "low risk" calls.

[other green calls for thia include: artichoke, tobacco, peanuts, sod, christmas trees and other outdoor residential (eg crack and crevice)]

## Summary of Risk Conclusions for Foliar Applications

| Crop Group or Crop | Imidacloprid | | Clothianidin | | Thiamethoxam | | Dinotefuran | |
|---|---|---|---|---|---|---|---|---|
| Cotton | Strong | | Strong | | Strong | | Strong | |
| Cucurbit Vegetables | | | Strong | | Strong | | Moderate | |
| Citrus Fruits | Pre-Strong | Post-Weak | | | Pre-Strong | Post- | | |
| Pome Fruits | Pre- | Post-Weak | Pre- | Post- | Pre-Strong | Post- | | |
| Stone Fruits | Pre- | Post-Weak | Pre- | Post- | Pre-Strong | Post- | Pre-Strong | Post- |
| Tree Nuts | Pre- | Post | Pre- | Post- | Pre-Strong | Post- | | |
| Tropical Fruits | Pre-Strong | Post-Weak | Pre- | Post- | Pre-Strong | Post- | | |
| Berries/Small Fruits | Pre-Strong | Post- | Pre-Strong | Post- | Pre-Strong | Post- | Pre-Strong | Post- |
| Root/Tubers Vegetables* | Weak | | Weak | | Weak | | Weak | |
| Fruiting Vegetables* | Strong | | | | Strong | | Strong | |
| Herbs/Spices | Weak | | | | Weak | | | |

* denotes call is for honeybee attractive crops within the crop group



The next few tables summarize the risk calls for agricultural crops. Again, these are based on Tier II colony level risks.

This table summarizes the risk conclusions for foliar applications. Red cells are risk, green cells are low risk, and gray cells are not registered. As with the low risk calls, for orchards (which encompasses citrus, pome, stone and tree nuts) and berries and small fruits, risk calls are distinguished for pre-bloom vs. post-bloom applications. Note that most of these calls were "uncertain" in the preliminary assessments due to gaps in the residue database. Bridging really allowed us to make them all green or red. This table also identifies the strength of evidence for the risk call in black text.

Overall, cotton, cucurbits, pre-bloom orchard (where registered), pre-bloom berries and small fruits, and honey bee attractive fruiting vegetables were the strongest evidence of risk for all chemicals.
In contrast, post-bloom applications were generally low risk or where risk was possible, they were at the weakest strength of evidence.

# Summary of Risk Conclusions for Soil Applications

| Crop Group or Crop | Imidacloprid | Clothianidin | Thiamethoxam | Dinotefuran |
|---|---|---|---|---|
| Cotton | Moderate | | | |
| Cucurbit Vegetables | Strong | Moderate | Moderate | |
| Citrus Fruits | Pre- Strong<br>Post- Moderate | Pre-<br>Post- Moderate | Pre- Strong<br>Post- Weak | |
| Pome Fruits | Pre-<br>Post- Weak | | | |
| Stone Fruits | Pre-<br>Post- Weak | | | Pre- Weak<br>Post- |
| Tree Nuts | Pre-<br>Post- Moderate | | | |
| Tropical Fruits | Pre-<br>Post- Weak | | | |
| Berries/Small Fruits | Pre- Strong<br>Post- | Pre-<br>Post- | Pre- Strong<br>Post- | Pre- Moderate<br>Post- |
| Root/Tubers Vegetables* | Weak | Weak | Weak | Weak |
| Fruiting Vegetables* | Strong | | Moderate | Weak |
| Herbs/Spices | Weak | | | |

* denotes call is for honeybee attractive crops within the crop group



Here is the table summarizing risk conclusions for soil applications. Where the foliar applications are mostly strong evidence of risk, the soil applications are more frequently moderate and weak evidence. This is because, as you may recall from our previous discussion of the general trends in residue data, residues from soil applications tend to be lower than foliar applications (although they generally do persist for much longer).

# Risk Calls – Non-Ag Uses

- Ornamentals and forestry
  - Strongest evidence of risk for ornamentals (all chemicals) and forestry (imi, dino)
  - Incidents for IMI, CLOTHI, and DINO

- Turfgrass (residential): moderate evidence of risk for all chemicals
  - Residues from open literature study with IMI and CLOTHI
  - Based on the assumption of flowering weeds on residential lawns



For non-agricultural ornamentals and forestry uses, we have limited residue data are available for IMI (soil), THIA (foliar and soil), and DINO (foliar and trunk injection). Ornamental plants are of known pollinator attractiveness-- just think about observing bees in your or neighbors gardens.
In addition, with regard to ornamental trees and forestry uses, various tree species are considered bee attractive, e.g., maple, tupelo, black locust, and linden.

We also have open literature (article by Hill and Webster, 1995) that discusses the potential economic benefits of combining apiculture and forestry operations as many of commercially valuable trees produce attractive nectar and pollen that are available during early spring, when other bee resources may be limited.

For ornamentals and forestry uses, despite some uncertainties in our ability to extrapolate from one chemical to another, the residue levels are in the PPM range. These large exceedances are likely much greater than any chemical specific influence we would see and lead us to conclude risk with the strongest weight of evidence for all chemicals.

The assessment for residential turf assumes that bee attractive weeds are present and flowering during application.
For residential turf uses, while residues are also in the PPM range immediately after application (based on data from an open literature study), they decline quickly and there is uncertainty related to the assumption that flowering weeds are present on residential lawns. For non-residential turfgrass uses (e.g. golf courses), we assume that flowering weeds are not present.

# Risk Conclusions for Other Bee Species

- Comparison of tox data and previous analysis of exposure indicate that honeybees are an appropriate surrogate for other bee species (bumblebee, etc.)
  - Conclusion of risk for honey bees extend to other bee species
  - Low risk calls for honey bees may be risk for other bee species
    - *e.g.,* potatoes (root and tuber crop group), tomatoes (fruiting vegetable group)



We also had some qualitative tier I individual bee data for other bee species, including bumble bees and some solitary bee species and this data indicated similar sensitivity for those species as for honey bees. Additionally, we also had some qualitative Tier II colony level data for bumble bees that also suggested they were of reasonably similar sensitivity at a colony level as honey bee colonies.

So, overall we consider honey bees to be an appropriate surrogate at the individual level for non-apis bees. And we also consider them an appropriate surrogate at the colony level for non-apis bees that form colonies (e.g. bumble bees)

Therefore, where we have called risk for honey bees, we are comfortable extrapolating that risk call to other bee species

Where we have called low risk for honey bees, the call does not necessarily extend. For example:

Fruiting vegetable call was low risk for honey bees, based on lack of attractiveness, but the conclusion for some crops, such as tomato, would be "Risk" for non-Apis. In the case of tomato, it produces attractive floral matrices to bumble bees and in fact they are brought in to commercially pollinate tomatoes in greenhouses, so exposure can definitely occur and risk for BB would be high based on the empirical residues in tomato.

This risk differential between the risk call for apis and non-apis occurs most frequently in the root and tuber crop group and the fruiting vegetable crop group.

# Ecological Risk Assessment Conclusions for Other (non-bee) Terrestrial Organisms

**Terrestrial Plants:**
- Low risk for all uses

**Birds and mammals:**
- *Foliar and soil uses:* Acute/chronic risk concerns for imi and clothi

- *Seed treatments:*
  - Acute and chronic risk concerns for imi, clothi and thia
  - Risk conclusions were refined considering seed size and % of diet to reach the level of concern
    - Greatest potential risk for uses on small seeds that require consumption of only a few seeds to reach LOC (*e.g.*, lettuce, sugarbeet)
    - Potential for risk for uses on large seeds that require consumption of only a few seeds to reach LOC, but seed size is too big for certain small species of birds (*e.g.*, passerine consumption of corn seed)
    - Lowest potential risk for uses with large seeds that require consumption of more seeds to reach LOC
  - Dino is not registered for seed treatment



For terrestrial plants, all uses were low risk.

For birds and mammals, acute and chronic risk was identified for some foliar and soil uses for IMI and CLOTHI, but contrary to our conclusions for bees, where seed treatments had the least risk, for birds/mammals seed treatments had the greatest risks through an animals consumption of the treated seed.

Because the RQ approach conservatively assumes 100% of the avian/mammalian diet comes from seeds, we refined these assessments and risk conclusions based on seed size and % of an animal's diet to reach a level of concern. This allowed for certain use patterns to be grouped into a "higher risk" category for mitigation considerations. I also want to note that we received comments on the potential for exposure to spilled treated seed, most notably from MN DNR and University of Minnesota/EPA? researchers (they have also was recently published this work), that confirm the potential for seed treatment exposures. This study also documented large amounts of seed spillage and documenting birds/mammals consuming treated seed (both at the spills and otherwise).

The general conclusions from risks posed by seed treatments are that:
1. Seed size driving some risk conclusions:
Lettuce, sugarbeet, (only few needed, <1% diet, possible to be ingested by all species)

2. Few seeds needed, but seed size too big for small/med passerines. Passerines or songbirds make up 75% of the species observed to visit Ag fields. Corn, seeds the size of cotton (small birds only). That said, larger birds and other non-songbird birds (e.g. game birds like the lesser prairie chicken) will definitely eat seeds of those sizes.

3. Use Patterns and size class of lower concern
Larger percentage of diet (>10%), more seeds to consume to reach the LOC (e.g. rates used on soybean are much lower)

Tie back to the overall usage of these chemicals, the ones that have the greatest risk are vegetable seed treatments that tend to have lower use. The most frequently used seed treatments (corn and soybean) still have risk, but either require a greater proportion of diet (soybean) or are larger seeds that passerine birds are unlikely to consume many of, but may pose a greater danger to other taxa (prairie chickens and sand crane are notable listed species that would be likely to consume these seeds).

Registrants have agreed that seed spillage is a problem and have suggested stewardship activities and advisory label language. In their public comments and in meetings we've had with them, they have generally disagreed however about the attractiveness of treated seed to wildlife, suggesting in fact that birds won't consume many treated seeds including soybean. However, historically and even still today, Japanese farmers used scarecrows in soybean fields precisely to try scaring birds away and of course in the US many farmers use anthraquinone as a bird repellent on their fields.

# Ecological Risk Assessment Conclusions for Aquatic Organisms

**Fish and Aquatic Plants**:
- Low risk for all uses

**Aquatic invertebrates:**
- Acute and chronic risk concerns for all 4 chemicals identified in preliminary risk assessments
- Additional toxicity data (Raby *et al*. 2018) submitted during public comment period allowed for comparison of risks across chemicals
  - Comparison of risk incorporates not just toxicity, but also varying application rates and fate characteristics for each chemical
  - IMI, CLOTHI, and DINO have similar risk profiles (RQs within 10x)
  - THIA has lower risks (due to less sensitive tox endpoints)
- Measured concentrations are greater than toxicity values, indicating risk



For fish and aquatic plant risks are low.

Our assessments identified that for aquatic inverts, there are acute and chronic risk concerns for all four chemicals and I'll note that chronic risks are the driver. Acute risks are based on lethality while chronic risks are based on effects on survival, growth, reproduction and for aquatic insects, specifically, emergence to adult form. Difficult to compare the chemicals at that time as the quality and quantity of data available was really varied, form imidacloprid that had well over a dozen aquatic sp. tested, to dinotefuran that was only tested on waterfleas (zooplankton) which are known to be relatively insensitive to neonics.

The additional open literature data from Raby (research out of the University of Guelph in Ontario under the auspices of the Ontario Ministry of the Environment to develop water criteria) was very helpful because she looked at effects of all 4 chemicals on 22 aquatic invert species for acute effects and then picked the two most sensitive of those (a midge and a mayfly) to do chronic testing, again with all 4 chemicals. This allowed us to make comparisons as to the toxicity of each chemical on an apples to apples basis, eliminating normal sources of variability that we usually have to consider when comparing toxicity across different chemicals such as lab and study conduct variability.

We took the Raby data and made comparative risk conclusions by looking at that data in comparison to the application rates and fate characteristics of each chemical. Based on this comparative analysis, IMI, CLOTHI, DINO are similar (Dino had less tox than the other two, but has higher app rates) while thia had lower risks.

Measured concentrations in water from monitoring studies are greater than toxicity values, confirming potential risk

Measured concentrations from monitoring data are greater than tox values.

# New Data Set – Guelph (Raby *et al.*) Aquatic Invert. Toxicity Data

- Large acute and chronic datasets across all 4 neonics (and acetamiprid)
- Allowed for apples-to-apples comparison of toxicity data across the 4 neonics, accounting for lab and study conduct variability
- 22 species tested for acute lethality, resulting in a large range of species' sensitivities.
  - 2 most sensitive acute species tested for chronic
- Tested species did not include the most sensitive species identified for imidacloprid
  - RQs for the other neonics may be higher if all had used this species



We also received as part of the comment period data from Guelph, which has since been published (2018). The Raby et al. study represents a large acute and chronic toxicity dataset across the four neonics (as well as acetamiprid) that allowed for an apples-to-apples comparison, accounting for lab and study conduct variability. There were 22 species included in the acute tests that included a range of species. The 2 most sensitive species from the acute test were then used in the chronic tests (the midge and a mayfly species). However, I'll note that the tested species did not include the most sensitive species identified for IMI.

# Aquatic Monitoring Data

- Sourced primarily from Water Quality Portal (multiple databases within)
  - Generally non-targeted in nature
  - Some targeted open literature data available for imidacloprid
- For imi, clothi, and thia:
  - Monitoring values similar to modeled data
  - Acute and chronic risk indicated

| Chemical | # Samples | % Detection Frequency | Highest concentration (µg a.i/L) | Chronic Endpoint from Risk Assessment (µg a.i/L) | Chronic Endpoint from Raby et al (µg a.i/L) | % of Monitoring Values Exceeding Most Sensitive Endpoint |
|---|---|---|---|---|---|---|
| Imidacloprid | 8,418 | 27% | 12.7 | 0.01* | 0.156** | 14% |
| Clothianidin | 1,801 | 12% | 1.34 | <0.5 | 0.31** | 3% |
| Thiamethoxam | 3,005 | 9% | 4.37 | 0.74** | 6.3** | 0.13% |
| Dinotefuran | 1,316 | 30% | 11.7 | 10,000++ | 3.1** | 0.23% |

* Mayfly (*Caenis horaria*)
** Midge (*Chironomus dilutus*)
\+ Mayfly (*Neocloeon triangulifer*)
\++ Daphnid (*Daphnia magna*)

INTERNAL DELIBERATIVE - DO NOT RELEASE



In addition to the comparisons to modeled data, it is important to note that there is a substantial monitoring data set available for the neonics. It is mportant to note that there is overlap of observed monitoring values with modeled data as well as aquatic endpoints (especially when considering the Raby et al data). This supports the potential for exposure and effects in the environment.

Caveat % of monitoring values exceeding most sensitive endpoint: we are comparing a daily sampled value and may not be representative of a chronic exposure.

# Overall Ecological Risk Conclusions

- **Final bee assessments**:
  - Risk to bees for foliar and soil treatment is greater than seed treatment
  - Highly refined assessments that are data-rich and allow for increased levels of realism and refinement
    - Include new methods for incorporating pollen exposures and crop group residue bridging
    - Responsive to public comments from USDA, Industry, Academia
  - Risk depends on use site, application method and chemical specific factors

- **Non-bee assessments:**
  - Risks to birds/mammals greatest from seed treatment uses
  - Risks to aquatic invertebrates greatest from foliar and soil and least from seed treatment
    - Incorporates recently submitted data that allows for comparative risk analysis
    - Potential risks from IMI, CLOTHI, DINO are greater than THIA

26

These RAs considered both Ag and Non-Ag Use sites (e.g. Ornamentals)

We found that Fol>Sol>Seed Treatment
Potential Impacts on our Pollinator Protection Goals of Pollination Services and Species Biodiversity
Note that for seed treatments, we did not quantitatively consider risk from abraded seed dust off.
Highly Refined RAs
Include new methods, responsive to public comments

Non-bee: Terrestrial: Most risk is from seed treatment risk to birds/mammals (all ai but dino).
Non-bee Aquatic: Risk is to Aquatic Inverts and is from all use patterns, but: Fol>Sol>Seed
Using newly submitted data from UGuelph we were able to do a comparative risk analysis between the ai's.
Found that Imi & Clothi highest, dino similar (dino had much less toxicity, but much higher app rates and so overall similar) and thia significantly less.

# Other Recent Regulatory Assessments

- PMRA recently (April) released final pollinator assessment and mitigation decisions for IMI, CLO, and THIA
  - Seed treatment conclusions consistent with those of EPA (low pollen/nectar exposure)
  - Cancels or restricts specific application methods and timing of certain use pattern
    - Cancels foliar uses on: Pome, Stone, some Tree nuts (IMI), Berry (CLOTHI), Outdoor attractive ornamentals (THIA), Turf (CLOTHI), some Herbs (IMI)
    - Cancels soil uses on Low Growing Berry (THIA), Outdoor attractive ornamentals (THIA/IMI), Fruiting Vegetables, Cucurbits (THIA), Legume (IMI), some Herbs (IMI)
    - Timing restrictions for foliar applications (too many to list)
- EFSA has released non-seed treatment RAs(2015) & updated seed treatment RAs (2018)
  - Seed Oral Route: IMI and CLOTHI are low risk from pollen and nectar residues, THIA inconclusive
  - Seed Dust-off is high risk for IMI, CLOTHI and THIA
  - Foliar Uses: High Risk to bees for pre-bloom uses. Low risk to bees for post-bloom uses.

Overall, our opinions with Canada's PMRA on the science were very similar. They found that seed treatments posed low risk to bees based on low pollen and nectar exposure and that risks were significant for foliar and soil treatments. It is worth noting that they used the same method for accounting for pollen exposures that we used in our preliminary risk assessments (not the total dietary approach we now used).

As such, PMRA decided to cancel many foliar and some soil treatments. Seed treatments were to receive advisory language regarding BMPs and fluency agent requirements to limit seed dust off.

By background on EU actions, in 2013, they prohibited neonicotinoid seed, soil and foliar applications on crops attractive to bees and cereals, except for greenhouse uses, winter cereals and post-bloom applications. EU then commissioned EFSA to conduct risk assessments for their uses.

# EFED Neonicotinoid Chemical Teams

| Chemical | EFED Branch | Eco | Fate |
|---|---|---|---|
| Clothianidin | ERB 6 | Michael Wagman | Chuck Peck |
| Thiamethoxam (combined document) | ERB 1 | Kris Garber<br>Ryan Mroz | Chris Koper |
| Imidacloprid | ERB 5 | Keith Sappington<br>Meghann Niesen<br>Hannah Yingling | Mohammed Ruhman |
| Dinotefuran | ERB 3 | Elizabeth Donovan | Rochelle Bohaty |
| Coordination and supporting roles | | Colleen Rossmeisl<br>Frank Farruggia<br>Monica Wait | |



Make sure to thank Elizabeth for all her work and point out she just gave birth! And also Colleen for her work on the Monte Carlo

# EFED Back-pocket Slides

# Preliminary Bee RAs - Major Public Comments

- Comments that were addressed through modification of the risk assessment
  - Criticism of "bee bread" method and alternative suggestions
  - Lack of non-agricultural use risk assessment
  - Assessments were not adequate due to numerous "Uncertain" calls
- Comments on lack of assessment for less-typical exposure routes
  - Seed dust, soil exposure, drinking water, guttation fluid
- Other substantive comments that did not result in changes to the risk assessment (not exclusive to neonics)
  - Assessments do not consider mixtures, cumulative effects, or synergy
  - Honeybees are not appropriate surrogates
  - Not enough consideration for studies that include sublethal effects or non-apical endpoints (*e.g.,* immunosuppression, foraging ability, biochemical changes)




This slide summarizes the major categories of public comments received on the preliminary bee risk assessments. While these comments are generic to the four neonics being assessed, there are chemical-specific comments that have been incorporated into the risk assessments as appropriate. Major commenters were USDA, registrants, various crop groups, non-profits, and state agencies.

There were several comments that were addressed through modifications to the risk assessment. These included: criticism of the "bee bread" method and alternative suggestions for how to estimate exposure for the Tier II analysis. These comments informed development of the new method for estimating exposure. There were comments that the risk assessments did not consider non-ag uses; these uses are considered in the final assessments (risk calls will be discussed later). And finally, there were comments that the assessments were not adequate because of the numerous "uncertain calls". These calls in the preliminary assessments were due to gaps in the dataset, mainly for the tier II assessment. Since the drafts, we have received new colony feeding studies for the chemicals and residue data that have allowed us to update our higher tiered exposure assessment.

There were also comments on the lack of quantitative assessment for some of the less-typical exposure routes, such as, seed dust, soil exposure, drinking water, and guttation fluid. These routes are discussed qualitatively in the assessments both because the potential exposures are substantially less than those from dietary and contact exposure and because there aren't methods to quantify them. Of all of these less-typical routes, the most relevant is seed dust as there are numerous incidents associated with this type of exposure. This is being addressed through stewardship.

And finally, there are other substantive comments that did not result in changes to the risk assessments. These are not exclusive to neonics and, ultimately, are not persuasive. Most of them relate to policy decisions and are being addressed with other work (e.g., synergy).

# Non-bee RAs – Major Public Comments

- Consumption of treated seeds by birds/mammals
  - Not sufficiently protective
    - Study from Univ of MN – > 25% of $LD_{50}$ ingested, neurological signs
    - Study from Univ of Saskatchewan showing weight loss/disorientation
  - Too conservative
    - Single food source, max load, every day
- Consideration of synergistic/cumulative effects of neonicotinoids
- Increased consideration of monitoring data, only consider habitats suitable for aquatic organisms, don't use foreign data
- Underestimation of runoff from treated seeds
- No accounting for residential uses and impacts to POTWs



EPA received several comments on the aquatic and terrestrial (non-bee) taxa, including those related to consumption of treated seeds, consideration of synergistic and cumulative effects, monitoring data, underestimation of runoff from treated seeds, and impacts from residential uses on POTWs,

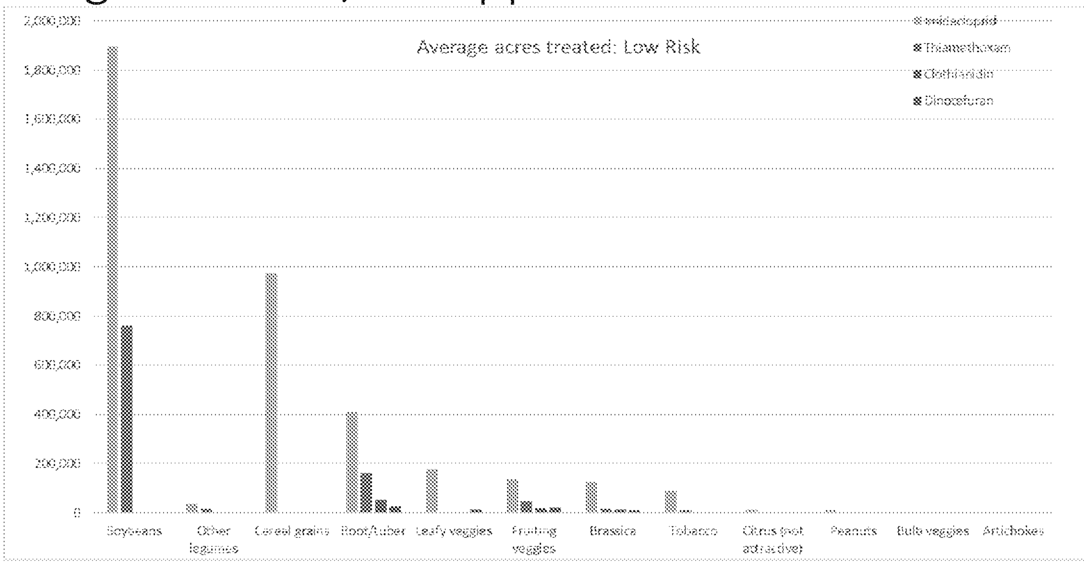
[Not sure if treated seeds data were considered

Monitoring data – monitoring data not sampled frequently enough to use alone. Habitats may discharge into receiving waterbodies that do harbor aquatic organisms. Foreign data provide line of evidence that neonics can contaminate waterbodies.

Underestimation of seed runoff - new seed treatment memo, EECs revised

Residential uses on POTWs – use of down-the-drain model require production volumes, can't parse out what is used for ag purposes and what is used for residential uses. Consider ag EECs as surrogates for residential uses when looking at mitigation options.]

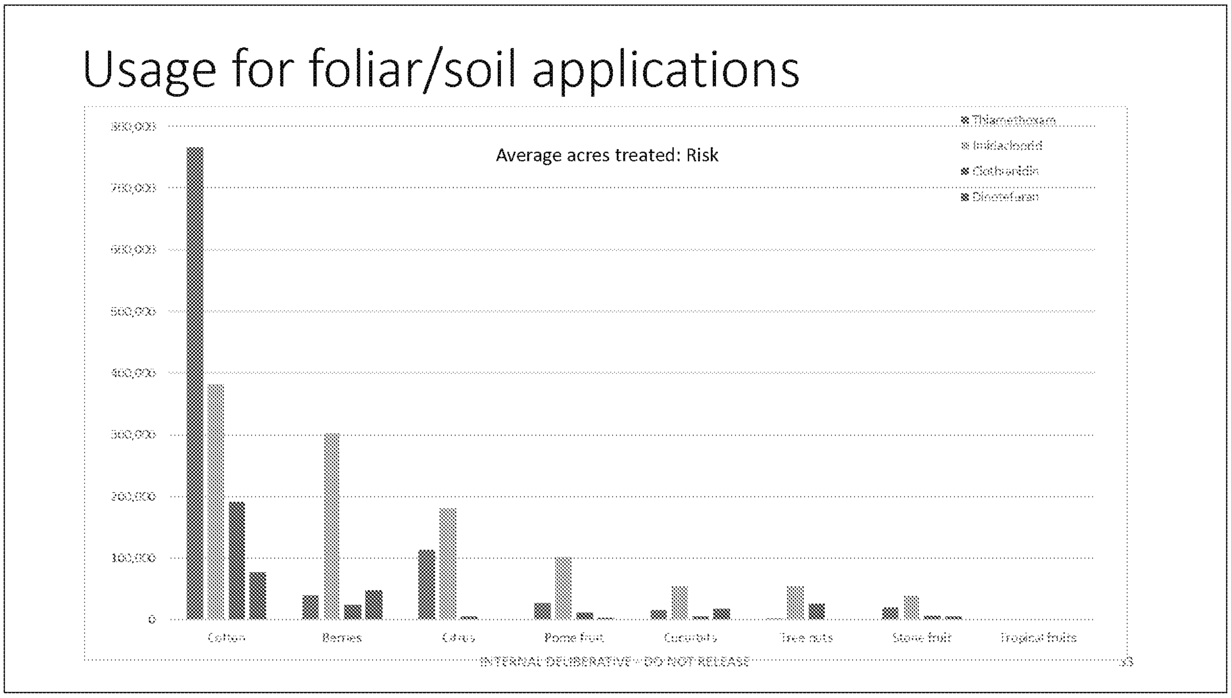
# Usage for foliar/soil applications




INTERNAL DELIBERATIVE - DO NOT RELEASE

32

Moving on to the foliar and soil applications, this figure shows the average acres treated (calculated the same was as for seed treatments) for all of the low risk crops/crop groups. For foliar/soil aps, the most usage is on soybeans, cereal grains. Take note of the y-axis before we transition to the next slide.




This shows the average acres treated for the risk crops. These data are for uses that have at least one red risk call so there are some nuances that don't translate, but in general, the crops with the highest acres treated are cotton, berries, and citrus. If you recall the scale from the previous slide you can see that the acreage for the risk crops is substantially less than the acreage for the low risk crops.

[For some of the orchard crop data, it is unknown whether usage was pre- or post- bloom. So, some of these acres treated may be green. E.g., clothi use on pome stone and tree nuts.]

# Hazard Comparison—Tier I Endpoints

| Endpoint | Imid | Clothi | Thia | Dino |
|---|---|---|---|---|
| **Acute Contact LD50 (adult) µg/bee** | 0.043 | 0.0275 | 0.025 | 0.024 |
| **Acute Oral LD50 (adult) µg/bee** | 0.004 | 0.0037 | 0.0044 | 0.0076 |
| **Chronic Oral NOAEC (adult) µg/bee/d** | 0.001 | 0.00036 | 0.0029 | 0.0015 |
| **Chronic Oral NOAEC (larvae) µg/bee/d** | 0.018 | No dose data (diet only) | 0.0043 | <0.0325 |

# Comparison of Tier II CFS results: sucrose-based endpoints (ppb)

| Chemical | NOEC | LOEC | Effects at LOEC |
|---|---|---|---|
| Imidacloprid | 23 | 48 | ↓Adults, Pupae, Pollen, Honey |
| Clothianidin | 19 | 35.5 | ↓ Adults, Eggs, Pupae, Pollen |
| Thiamethoxam | 44 | 81 | ↓ Larvae, Pupae, Pollen |
| Dinotefuran | 124 | N/A | None |



Endpoints are based on consistent effects over multiple CCAs
Imi, Clothi and Thia, all had consistent impacts to brood and pollen, with imi and clothi having impacts to adults at similar LOEC.

Dino did not have any persistent effects, however there was an ~20% decrease at the highest treatment group at 1 CCA.
For clothi and thia we actually had 2 studies submitted each bc the first studies didn't successfully overwinter in control hives. However, they did in the 2nd set of studies and in both cases (and also for IMI and DINO), overwintering success did not affect the endpoint. In other words, the most sensitive impacts were on adults, brood production and pollen food storage after application and not on colony survival after overwintering. However, these consistent in-season effects have implications for our pollinator protection goals, particularly on pollination services (if you have less adults or these adults are less effective at foraging then that impacts that protection goal.

# Lines of evidence for derivation of weighting factor

## 1. Colonies consume more nectar than pollen

A. Relative food consumed by colonies based on BeeREX food consumption rates

- Colonies consume **25x** more nectar than pollen on daily basis
- Based on numbers of larvae and adults measured in controls of CFSs

B. Food consumed in control colonies of similar CFS (clothianidin)

- Over 6 week period, colonies consumed **21x** more sucrose than pollen
  - pollen CFS: 1.5 kg
  - sucrose CFS: 32 kg

C. Seeley (1985): colonies consume 20 kg pollen + 60 kg honey (160 kg nectar)

- Colonies consume **8x** more nectar than pollen in a year
- Based on estimates of amount of pollen needed to rear brood
- Assumptions related to "unmanaged" hives in New England

# Lines of evidence for derivation of weighting factor

## 2. Colony level endpoints for sucrose (nectar) are lower than for pollen

A. Quantitative: Clothianidin sucrose (MRIDs 49836101 and 50312501) and pilot pollen (MRID 50478501)
   - Sucrose based effect levels is **19x lower** than pollen concentrations (with comparable effects)
   - This is the most robust pollen feeding study available

B. Qualitative Imidacloprid definitive sucrose (MRID 49510001) and literature pollen (Dively 2015) studies
   - Sucrose endpoint is **2.1x lower** than pollen endpoint
   - Dively study is "qualitative"

C. Qualitative: Imidacloprid pilot study (NC)
   - No effects in pollen at 50 and 200 ppb; effects in sucrose at 50 ppb
   - Suggests that effects are observed in sucrose at levels that are ***at least*** **4x lower** than p

# Conclusions in weighting factor derivation

- Honey bee colonies consume more nectar than pollen
  - If concentrations in pollen and nectar are equal, dose from nectar will be greater
- Available information suggest that on a concentration basis, colony level endpoints for nectar should be lower than pollen
- Route of exposure does not appear to influence toxicity
  - When sucrose and pollen based CFS NOECs and LOECs are converted to dose, they are within same order of magnitude (<2.6x different)
- Three lines of evidence indicate that difference in contribution of colony's dose from pollen is 20x less than that of nectar
  - Final equation:

$$\boxed{C_{total} = C_{nectar} + \frac{C_{pollen}}{20}}$$





This factor has been used by Sulfoxaflor already in their risk assessment that went out recently.

# Data Bridging Needs vs. Available Data—Seed and Trunk Injection

| Crop Group | Application Method | Chemical | | | |
|---|---|---|---|---|---|
| | | Imidacloprid | Clothianidin | Thiamethoxam | Dinotefuran |
| **Root/Tuber Vegetables** | **Seed** | | | | |
| **Legumes** | **Seed** | Soybean | Soybean | Soybean | |
| **Cucurbits** | **Seed** | Melon* | Melon* | | |
| **Cereal Grains** | **Seed** | Corn | Corn | Corn | |
| **Forage, fodder, straw, hay (alfalfa)** | **Seed** | | | | |
| **Peanut** | **Seed** | | | | |
| **Oilseed** | **Seed** | Sunflower, Canola | Cotton, Sunflower*, Canola | Cotton, Sunflower*, Canola | |
| **Stone Fruit** | **Trunk Injection** | | | | Cherry |

*only studies available are for European data

# Data Bridging Needs vs. Available Data--Soil

| Crop Group | Chemical (Soil Application) | | | |
|---|---|---|---|---|
| | Imidacloprid | Clothianidin | Thiamethoxam | Dinotefuran |
| **Root/Tuber Vegetables** | | Potato | | Potato |
| **Legumes** | | | | |
| **Cucurbits** | Melon, Watermelon | Melon, Pumpkin, Cucumber, Squash | Melon, Pumpkin, Cucumber, Squash | Melon, Pumpkin, Cucumber, Squash |
| **Citrus Fruits** | Orange, Mandarin, Grapefruit | Orange, Lemon | Orange | |
| **Pome Fruits** | Apple | | | |
| **Stone Fruits** | Cherry, Peach, Plum, Apricot | | | |
| **Berries/Small Fruits** | Strawberry, Blueberry | Grapes | Strawberry | |
| **Cereal Grains** | | Corn** | | |
| **Tree nuts** | * | | | |
| **Oilseed** | Cotton | | | |
| **Fruiting Vegetable** | Tomato | | Pepper, Tomato | Pepper |

* Except almond for IMI; ** Experimental Use permit for in-furrow soil application for corn.

# Available Crops for Bridging Strategy-Foliar

| Crop Group | Chemical (Foliar Application) | | | |
|---|---|---|---|---|
| | Imidacloprid | Clothianidin | Thiamethoxam | Dinotefuran |
| **Root/Tuber Vegetables** | | Potato | | |
| **Legumes** | Soybean | | Soybean | |
| **Cucurbits** | Watermelon | Pumpkin | Pumpkin, Cucumber | Pumpkin, Cucumber |
| **Citrus Fruits** | Orange | | Orange | |
| **Pome Fruits** | Apple | Apple | Apple | |
| **Stone Fruits** | Cherry, Peach, Plum, Apricot | Peach | Cherry, Peach, Plum | Cherry, Peach |
| **Berries/Small Fruits** | | Grape | Strawberry, Blueberry, Cranberry | Blueberry, Cranberry |
| **Cereal Grains** | | | ** | *** |
| **Tree nuts** | * | Almonds | | |
| **Oilseed** | Cotton | Cotton | Cotton | Cotton |
| **Fruiting Vegetables** | Tomato | | Tomato | Tomato |
| **Herbs and Spices** | | | | |

* Except almond for IMI; ** registered for barley only (not bee attractive); *** registered for rice only (not bee attractive)

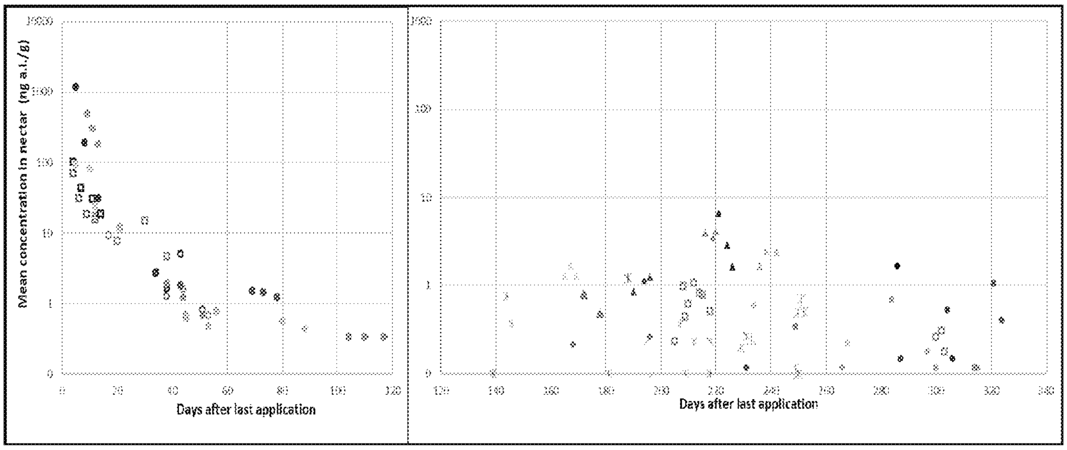
This slide illustrates how we are assessing risk at the crop group level by application type (in this case foliar)

Yellow = registered, but no ai-specific data
Gray = not registered

Data generally supported extrapolation of residues across neonics, but not among application methods.
Within an application method and crop group, residues extrapolated among crops
In absence of data for a given crop group, considered all data within an application category (e.g. to evaluate foliar risks to herbs and spices, we used all the foliar data from all the herbaceous crops)

Our coverage here across crop groups wasn't happenstance, this was by design.
Things we looked at for bridging: Can you bridge across crops in crop group? (e.g. Thia pumpkin and cucumber), Can you bridge across chemicals for a crop group (e.g. clothianidin and thiamethoxam cucurbits?) In these examples, the kinetics were similar and supported bridging across crops and a.i..

# Bridging Example—
# Orchard Crops, Foliar applications






Different shapes represent different ai's while different colors represent different crops and residues are normalized to a 0.1 lb ae/A application rate. In this case, looking at foliar applications to orchard crops we felt it made sense to divide the applications by timing, comparing pre-bloom applications (on the left, which generally had very high residues for more than a month following applictions) with post-bloom applications (on the right), which generally had very low levels of residues after more than 6 weeks following application. The important take home point is that where we had overlapping data by time, we generally didn't see large discrepancies between the levels of residues from different active ingredients or from different crops within the orchard crop group, which is an amalgamation of tree crop groups (tree nut, pome, stone and citrus tree crops).

<if needed>, on the left, we had data on citrus and pome fruits, while on the right, we had data on Pome, Tree nut, & Stone fruit

# Seed Treatment Residue Bridging – Conclusions

- Crop specific 90$^{th}$ percentile values (from all trials)
  - Separate values for corn, cotton, soybean and canola
    - Data bridged across chemicals
  - Tier I (refined)
  - Tier II (when needed)

- For crops with no seed treatment residue studies, available data for corn, cotton, canola and soybean were used to bridge to other crops
  - 90$^{th}$ percentiles used for all other crops, with adjustments for treatment rate



The recommendations based on the seed treatment bridging are: 1) for crops with available data, use the 90th percentile value from all chemicals. There are separate values for corn, cotton, soybean, and canola. These values are used to refine Tier I estimates, and Tier II only when needed (which was not very often). 2) for crops without data, the aggregate 90th percentile across all of the crops (i.e., corn, cotton, canola, and soybean) is used.

[90th percentile is the high end year/site conditions. 90th selected based on policy and level of protection we tend to pick. Consistent with aquatic EECs. Precedent.]

"this is what we used, based on residue bridging recommendations" MC

# Foliar and Soil Bridging – Conclusions

- Based on the bridging analysis, the following crop/crop groups are bridged across chemicals:
  - Cotton (THIA only)
  - Cucurbits
  - Orchards (Stone fruit, pome fruit, citrus, tree nuts, tropical fruit)
  - Berries and small fruits
  - Fruiting vegetables (*e.g.,* peppers)
  - Soybeans
- For crops/crop groups with insufficient data:
  - Cotton and cucurbit data used as surrogates
  - Relevant crop groups
    - Root and tuber (*e.g.,* sweet potato)
    - Fruiting vegetables (*e.g.,* okra and roselle)
    - Herbs and spices





Based on the bridging analysis for foliar and soil applications, cotton, cucurbits, orchards, berries and small fruits, and soybeans are bridged across all chemicals. A few things to note: cotton data is bridged across chemicals for THIA only because there was sufficient data for IMI, CLOTHI, and DINO to use chemical-specific data. Orchards represents an artificial grouping of various tree crop groups (e.g., citrus, stone, pome, tree nut). Residues are bridged across all orchard crop groups.

For crops/crop groups with insufficient data, using other crops as surrogates we have enough data to cover most of the crops that are registered with some degree of confidence.

{HED didn't have any issues with approach}

# Non-Ag Bridging – Conclusions

- Limited Ornamental data were available for imidacloprid, dinotefuran and thiamethoxam
  - Imidacloprid and Dinotefuran data were not comparable to other a.i.'s due to the way their application rates were described in study reports.
  - Thiamethoxam data were used as surrogates for all other a.i.'s
  - Residues in nectar alone from foliar applications = 100 - 1000s ppb
  - Residues in nectar alone from soil applications = 10 - 100s ppb

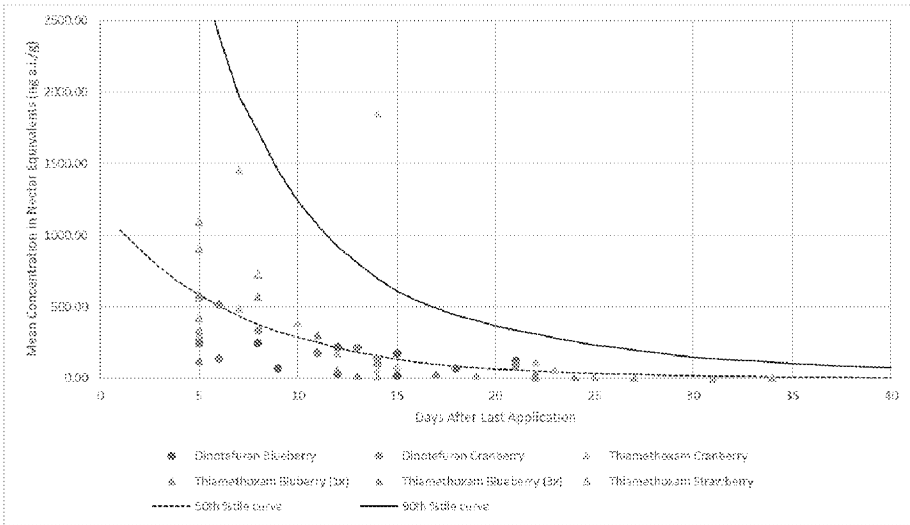
- Open Literature residue data on Turf for imidacloprid and clothianidin suggested the a.i. are similar with very high initial concentrations (>1000 ppb), but with rapid declines (~20 ppb by 3 weeks)



Residues remained above CFS endpoints for up to 3 weeks, which was the extent of the sampling period in the thiamethoxam ornamental dataset.
Turf has highest use rates for some ai (clothianidin)

talking point about clarifying the less-managed turf that contains bee-attractive plants (e.g., clover)

# Example Simulation: Berries foliar applications




INTERNAL DELIBERATIVE - DO NOT RELEASE

# Risk Calls

- Cotton
  - Foliar: IMI; CLOTHI; THIA; DINO
  - Soil: IMI
- Cucurbits
  - Foliar: CLOTHI; THIA; DINO
  - Soil: IMI; CLOTHI, THIA
- Orchards
  - Foliar Pre-bloom: IMI; CLOTHI; THIA; DINO
  - Foliar Post-bloom: IMI (except tree nuts)
  - Soil Pre-, Post-bloom: IMI; CLOTHI; THIA
  - Soil Pre-bloom: DINO
- Berries and Small Fruits
  - Foliar Pre-bloom: IMI; CLOTHI; THIA; DINO
  - Soil Pre-bloom: IMI; THIA; DINO
- Legumes
  - Soil: IMI
- Other Herbaceous Crops
  - Root and Tuber
  - Fruiting Vegetables
  - Herbs and Spices
- Seed Treatments
  - Turmeric: CLOTHI
  - Bean and Peanut: IMI
- Ornamentals and Forestry
  - Foliar/Soil: IMI; CLOTHI; THIA; DINO
  - Trunk Injection: IMI; DINO
- Turf (residential)



Moving to the risk calls... We'll walk through the details in the following slides, but risk calls were made for all of the uses shown here. As discussed previously, risk calls are based on residue values exceeding the NOAEC. However, all of the lines of evidence were used to characterize the strength of the risk call.

# Summary of Risk Conclusions for <u>Seed Treatments</u>

| Crop Group or Crop | Imidacloprid | Clothianidin | Thiamethoxam |
|---|---|---|---|
| Bulb Vegetables | | | |
| Leafy Vegetables | | | |
| Brassica Vegetables | | | |
| Legumes | Weakest (Beans) | | |
| Cereal Grains | | | |
| Oilseed | | | |
| Cucurbit Vegetables | | | |
| Root/Tubers Vegetables* | | Weakest (Turmeric only) | |

INTERNAL DELIBERATIVE - DO NOT RELEASE



* denotes call is for honeybee attractive crops within the crop group

Here is the table summarizing the risk conclusions for seed treatment uses. As you can see, most of the seed treatments are low risk, as we discussed previously, with the couple of exceptions noted here.

## Off-site Risk Conclusions—Spray Drift & Poultry

- Spray drift: off-field dietary risks to individual bees extend 1000 feet from the edge of the field

- Clothi, Thia and Imi poultry house uses risk based on Tier I
  - Risk call is based on treated poultry litter subsequently applied to an agricultural field
  - No residue data are available
  - Imi & Thia – No label specific restrictions for area treated or house treatments before cleanout
  - Clothi - Incorporates proposed mitigation scenarios from the registrant (does not change the risk call, but exposures are considerably reduced under these mitigations)



In addition to the Tier II risk conclusions there are Tier I conclusions that have not changed from the preliminary assessments, including conclusions for the clothi poultry and risks from spray drift.

Based on a Tier I analysis, for foliar applications, off-field dietary risks to individual bees exposed to spray drift extend 1000 feet from the edge of the treated field. There is uncertainty in this conclusion which includes: assumption of available attractive forage off field, use of individual level toxicity data, BeeREX default estimates for residues, and unrefined AgDRIFT™ modeling.

# Off-site Risk Conclusions--Seed Dust-Off

- Numerous Ag Area/Corn incidents have been reported for both chemicals in association with abraded seed coat dust drift off following corn planting
- Dust-off, while not quantitatively considered in this risk assessment, is considered a route of exposure
- The assessment includes language that the Agency will attempt to mitigate risks using BMPs and working with stakeholders in development of alternative technologies to reduce this exposure (consistent with Imidacloprid Risk Assessment language)





Fewer incidents have been reported since 2014. Is this due to BMPs, different weather conditions or some other cause (e.g. frustration by beekeepers)

# Refinements for Seed Treatments Avian Acute Risk

- RQs assume seeds = 100% of avian/mammalian diet and palatable
- Refinements: (1) seed size (passerines only), (2) % of diet = seeds @ LOC

**(1)** **Seed Size: Corn, soybean, potato**: seed considered too large for consumption by small & medium passerine birds; **Cotton** too large for small passerines

**(2)** **% of Daily Diet = Seeds @ LOC:**
- **Large birds:** ≥ 99% for **cotton**, **soybean**, **corn** (clothi), **potato** (imi);
- **Large mammals:** >96% for **soybean** (clothi & Imi); **cotton, sorghum, wheat, potato** (imi)
- Small birds and mammals: small veg seed: few seeds and low % of diet (10%)



Talking point - MN study on seed treatment exposures

Group use patterns in "higher risk" category

1. Seed size driving some conclusions:
Lettuce, sugarbeet, (only few needed, possible to be ingested)

2. Few seeds needed, but seed size too big (small/ed passerines)
Corn, soybean, cotton (small only)

3. Use Patterns and size class of lower concern
Larger percentage of diet, more seeds to consume

Tie back to SLUA, larger percentage of diet to reach LOC for major uses (corn, soybean, cotton)

Highlight relative ease of mitigating on small vegetable seeds (e.g. lettuce) by recommending bittering agent on seed coating

Uncertainties:
Terrestrial Risk: Assumes seed is palatable available for consumption
Aquatic Risk: > 2 cm assume no runoff [MLW – remove this talking point. Aquatic modeling of seed treatments was revised by Chuck.]
Actual seeding depth likely to be variable